REMARKS

In the Office Action of September 12, 2005, the Examiner rejected claims 28-39 under 35 U.S.C. § 102(e) and 35 U.S.C. § 103(a) and claims 28-39 under the judicially created doctrine of obviousness-type double patenting. Each of the rejections is addressed below.

Double Patenting Rejection

The Examiner has rejected claims 28-39 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Pat. No. 5,723,289. In response Applicant is submitting a Terminal Disclaimer to overcome this rejection.

Rejection under 35 U.S.C. § 102(e)

The Examiner has rejected claims 28-39 under 35 U.S.C. § 102 (e) as being anticipated by Eaton *et al.* U.S. Pat. No. 5,723,592 (the '592 Patent). In response to this rejection Applicant hereby submits a declaration under 37 C.F.R. § 1.132 showing that the invention disclosed but not claimed in the '592 Patent was derived from co-inventor Eaton of the instant application.

The Examiner has rejected claims 28-39 under 35 U.S.C. § 102 (e) as being anticipated by Eaton *et al.* U.S. Pat. No. 5,723,289 (the '289 Patent). In response to this rejection Applicant hereby submits a declaration under 37 C.F.R. § 1.132 showing that the invention disclosed but not claimed in the '289 Patent was derived from co-inventor Eaton of the instant application.

The declarations are submitted unsigned; signed versions will be submitted by way of a supplemental amendment and response when available. Withdrawal of the 35 U.S.C. § 102(e) rejection is respectfully requested.

Rejections under 35 U.S.C. § 103(a)

The Examiner bears the burden of establishing a prima facie case of obviousness. In determining obviousness, one must focus on the invention as a whole. *Symbol Technologies Inc. v. Opticon Inc.*, 19 USPQ 2d 1241, 1246 (Fed. Cir. 1991). The primary inquiry is: "Whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have had a reasonable likelihood of success . . . . Both the suggestion and

the expectation of success must be found in the prior art, not the applicant's disclosure." *In re Dow Chemical*, 5 USPQ 2d 1529, 1531 (Fed. Cir. 1988).

The Examiner has rejected claims 28 and 32-35 under 35 U.S.C. § 103(a) as being unpatentable over Ellington *et al.* (1992) Nature 355:850-852 in view of Hilvert *et al.* (U.S. Pat. No. 5,208,152) (the '152 patent). Regarding independent claim 28, the Examiner asserts that Ellington *et al.* teach a method of obtaining single-stranded DNA molecules capable of ligand binding that are isolated via selection and amplification *in vitro*. In addition, Ellington *et al.* teach that nucleic acid aptamers may be new catalysts for chemical transformations that are analogous catalytic antibodies. The Examiner asserts that the '152 patent teaches the use of a catalytic antibody to perform a Diels-Alder reaction. The Examiner further asserts that this reference teaches that it would be beneficial to find a specific catalyst for Diels-Alder reactions. From these references, the Examiner concludes that it would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to use the ligand binding nucleic acid apatmers of Ellington *et al.* to couple with a first reactant and catalyze the Diels-Alder reaction with a free reactant to produce a cyclohexene derivative product library with the added benefit of a significant enhancement of the rate of reaction. Regarding dependent claims 32-35, the Examiner asserts that Ellington *et al.* teach the use of DNA oligomers having conserved and random sequences (claim 32), the use of single stranded DNA (claim 33), and that different single stranded-DNA oligomers can be selected to fold into specific binding structures (claims 34 and 35). For the reasons discussed below, this Section 103(a) rejection is respectfully traversed.

The Ellington *et al.* reference, teaches a method of selecting nucleic acid ligands that bind specifically to a target from a pool of random sequences. The method taught by Ellington *et al.* for selecting these nucleic acid ligands is comprised of the steps of: preparing a pool of random DNA sequences, selecting the DNA sequences that bind to the target and amplifying these sequences *in vitro*. (Abstract, lines 1-4). Thus, to the extent that there is even a product library in Ellington *et al.*, that library is comprised solely of nucleic acids that bind to a specific target. The only diversity in such library is in the sequences of the nucleic acid ligands. It is suggested in the reference that the nucleic acid ligands selected may be able to serve as a catalyst for a subsequent reaction. (page 852, col. 2, last paragraph). The reference provides no actual

examples of the use of DNA ligands as catalysts for any reaction. Nor does the reference provide any suggestion or guidance as to the types of reactions that may be catalyzed by the selected ligands. The '152 patent as noted by the Examiner teaches the use of a catalytic antibody to perform a Diels-Alder reaction.

By contrast, the instant application is directed toward a method for forming a cyclohexene derivatized product library. The product library is formed by the reaction of a mixture of first reactants each coupled to a nucleic acid ligand with a mixture of free reactants. The first reactant may be either a diene or a dienophile. The reaction is facilitated by the nucleic acid ligands that are coupled to the first reactants. Thus, each library member is attached to the nucleic acid that facilitated its formation. The present invention does not require an initial selection for the nucleic acids that bind to the first reactants. The first reactants in the instant application are instead attached or coupled to the nucleic acid molecules in the randomized pool.

Applicant maintains that the Ellington *et al.* reference in no way teaches or suggests the Applicant's claimed method of producing a cyclohexene derivative product library. Rather, as noted above, Ellington *et al.* teach a method for selecting nucleic acid ligands that bind to a specific target and suggests that these ligands may be able to serve as a catalyst for a subsequent reaction. Thus, at the most Ellington *et al.* suggest that it might be obvious to try to use their method to identify a catalyst to some unidentified reaction. As noted by the Examiner, Ellington *et al.* do not specifically teach the use of a Diels-Alder reaction. In fact, Ellington *et al.* do not specifically teach or suggest the use of their method for any reaction. Ellington *et al.* merely provide that "DNA like RNA may be able to catalyse chemical transformations." (page 852, col. 2, last paragraph). Likewise, the '152 patent does not teach or suggest the method of the instant invention. This reference merely teaches an antibody capable of catalyzing one specific type of Diels-Alder reaction in which the diene is a five or six membered ring having a fugitive leaving group. (the '152 Patent, col. 18, lines 55-63).

For the reasons discussed above, Applicants do not believe that the cited references, either alone or in combination, render the method of the instant invention as set forth in independent claim 28 and dependent claims 32-35 obvious. Reconsideration is respectfully requested.

The Examiner has rejected claim 29 under 35 U.S.C. § 103(a) as being unpatentable over Ellington *et al.* in view of Hilvert *et al.* as applied to claim 28 above and further in view of Woo *et al.* (1991) J. Amer Chem. 113:55457-5459. Claim 29 of the instant invention is drawn to the method of claim 28 further comprising a linker group between the first reactant and the nucleic acid. The Examiner reasons that while neither Ellington *et al.* nor the '152 patent teach the use of linkers, Woo *et al.* teach the use of psoralen probes that are tethered to oligonucleotides. As discussed in detail above, the Ellington *et al.* reference, taken either alone or in combination with the '152 patent, does not teach or suggest the method of this invention. Woo *et al.* is merely cited as teaching linkers and therefore does not cure this defect. Reconsideration is respectfully requested.

The Examiner has rejected claims 30 and 31 under 35 U.S.C. § 103(a) as being unpatentable over Ellington *et al.* in view of Hilvert *et al.* and Woo *et al.* as applied to claim 29 above and further in view of Cload *et al.* (1993) J. Am. Chem. Soc 115:5005-5014 as defined by Jolly (1984) Modern Inorganic Chemistry, McGraw Hill. Claim 30 of the instant invention is drawn to the method of claim 29 wherein the linker has a size in the range of 10 to 1000 Å and claim 31 is drawn to the method of claim 30 wherein said linker is selected from PEG, polyvinyl alcohol, polyacrylates and polypeptides. The Examiner reasons that Cload *et al.* teach the use of oligonucleotide probes tethered to a PEG linker (claim 31) and the combination of Jolly and Cload *et al.* clearly establish the length of the linker taught by Cload *et al.* as being between 10 and 1000 Å (claim 30). As discussed in detail above, the Ellington *et al.* reference taken either alone or in combination with the '152 patent and Woo *et al.* does not teach or suggest the method of this invention and thus does not render it obvious. The Cload *et al.* and Jolly references do not cure this defect and thus do not render dependent claims 30 and 31 obvious. Reconsideration is respectfully requested.

The Examiner has rejected claims 36-39 under 35 U.S.C. § 103(a) as being unpatentable over Ellington *et al.* in view of Hilvert *et al.* and further in view of Verdine (PCT International Publication No. WO 93/ 14108). Claim 36 of the instant invention is drawn to the method of claim 28 wherein nucleic acid test mixture comprises nucleic acids having one or more functional groups as set forth in the claim. Claims 37 to 39 are drawn to the method of claim 36 wherein the functional group is positioned at the ribose ring (claim 37), the base (claim 38) or the

phosphate group (claim 39). Verdine is cited as teaching the attachment of functional groups at various positions of nucleic acids including the ribose position, the base of the nucleic acid and the phosphate group. As discussed in detail above, the Ellington *et al.* reference taken either alone or in combination with the '152 patent does not teach or suggest the method of this invention. The Verdine reference does not cure this defect and thus does not render dependent claims 36-39 obvious. Reconsideration is respectfully requested.

Applicant believes that the pending claims are now in condition for allowance. If it would be helpful to obtain favorable consideration of this case, the Examiner is encouraged to call and discuss this case with the undersigned.

This constitutes a request for any needed extension of time and an authorization to charge all fees therefore to deposit account No. 19-5117 if not otherwise specifically requested. The undersigned hereby authorizes the charge of any fees created by the filing of this document or any deficiency of fees submitted herewith to be charged to deposit account No. 19-5117.

Respectfully submitted,

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